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The role of platelet distribution width in the diagnosis of ischemic and hemorrhagic stroke

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Abstract

Aim: Current efforts to find diagnoses using simple and widely used indices of platelet activation have focused on the platelet activation caused by morphological changes, including both pseudopodia formation and spherical shape. The aim of this study was to evaluate the effect of PDW in differentiating ischemic and hemorrhagic stroke.

Material and Methods: The study included a total of 333 patients, of which 269 had ischemic stroke and 64 had hemorrhagic stroke. Demographic data of the patients such as gender and age, National Institutes of Health Stroke Scale (NIHSS), Glasgow Coma Scale (GCS) and the modified Rankin score (mRs) were recorded. Complete blood count parameters were also recorded and compared between the patients with ischemic and hemorrhagic stroke.

Results: The mean age of the patients was found to be 72.3±12.71 years in the ischemic stroke group and 69.27±14.39 years in the hemorrhagic group. The median neutrophil count was statistically significantly higher in the hemorrhagic stroke group (p=0.041). The median level of albumin was statistically significantly higher in the patients with hemorrhagic stroke (p=0.010). The median PDW value was determined to be statistically significantly higher at 14.9 (11.9-17.8) in the ischemic stroke group compared to 12.85 (11.33-17.03) in the hemorrhagic stroke group (p=0.009).

Discussion: As the PDW level was statistically significantly lower in patients with hemorrhagic stroke than in patients with ischemic stroke, it may be of value in distinguishing these two forms of stroke. However, further comprehensive, multi-center studies are needed to better understand the role of PDW in ischemic and hemorrhagic stroke.

Keywords

Cerebral Hemorrhage, Cerebrovascular Disorders, Platelet, Stroke

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Introduction

Stroke is a neurological disease characterized by blood vessel occlusion. The formation of clots in the brain interrupts blood flow, blocks arteries, and causes blood vessels to rupture, resulting in bleeding. This causes the sudden death of brain cells due to oxygen deprivation. Stroke is an important cause of disability, the prevalence of which is increasing in parallel with the growing world population. It is also the second most common cause of death worldwide [1], affecting approximately 13.7 million people per year and causing the death of approximately 5.5 million people [2].

The global burden of ischemic strokes is nearly 4-fold greater than that of hemorrhagic strokes [3]. Of all strokes, 87% are caused by ischemic infarctions [4]. In ischemic stroke, reduced blood flow to the brain causes embolism, resulting in severe stress and cell necrosis, after which the cellular contents leak into the extracellular space [5]. Hemorrhagic strokes, which have a high mortality rate, constitute 10-15% of all strokes. Blood vessels are ruptured in a hemorrhagic stroke due to brain stress and internal injury. Blood accumulates abnormally within the brain as a result of vessel rupture, and the toxic effects of a hemorrhagic stroke on the vascular system cause hemorrhage [6]. The primary causes of hemorrhagic stress are vasculature disruption, hypertension, and excessive use of anticoagulants and thrombolytic agents [2]. There are two types of hemorrhagic stroke, which are classified as intracerebral and subarachnoid. Comparison between ischemic and hemorrhagic stroke is difficult, as ischemic stroke is approximately 10 times more common [7].

Platelets are important for coagulation, atherosclerosis, immune response, and inflammation [8-10]. Platelet parameters have been extensively studied in the literature. Current efforts to find simple and widely used indices of platelet activation have focused on the platelet activation causing morphological changes in platelets, including both pseudopodia formation and spherical shape [11]. Platelet distribution width (PDW), which reflects the variation in platelets, functions as an indicator of platelet activation and function [12]. Higher PDW levels are related to cancer, type 2 diabetes, cardiovascular disease, and respiratory problems [13,14]. In addition, increased PDW values have been observed in individuals with serious illnesses [15,16]. Activated platelets release high expression levels of glycoproteins Ib and IIb/IIIa, contributing to stroke [17]. Although PDW and mean platelet volume (MPV) are both indicators of platelet activation, PDW is a more accurate indicator of platelet reactivity [18].

Generally, cortical infarctions, which can be easily diagnosed with imaging techniques, can be managed in emergency departments without any problems. However, there are still patients classified as having unspecified ischemic stroke. PDW can assist decisions about ischemic events. The aim of this study was to evaluate the value of PDW in differentiating ischemic and hemorrhagic stroke.

Material and Methods

Ethics Committee Approval

The institutional review board of our hospital approved the study protocol on February 22, 2022 (number: 2022/29). Since the study was retrospective, informed consent was not necessary. All procedures were applied in accordance with the 2013 update of the Declaration of Helsinki.

Study Design

The study included a total of 333 patients, of which 269 had ischemic stroke and 64 had a hemorrhagic stroke, who presented at the Emergency Department between August 01, 2021 and February 28, 2022. Patients <18 years old, those who received thrombolysis therapy combined with mechanical thrombectomy, patients with inflammatory disease, underlying hematological disease, autoimmune disease, pregnant women, those without complete blood count on admission, and those with incomplete data were excluded from the study.

The age and gender of the patients were recorded together with the National Institutes of Health Stroke Scale (NIHSS), the modified Rankin score (mRs), and the Glasgow Coma Scale (GCS) score. Complete blood count parameters were also recorded and compared between the patients with ischemic and hemorrhagic strokes.

Statistical analysis

Data obtained in the study were analyzed statistically using SPSS version 23.0 software (SPSS, Statistical Package for the Social Sciences, IBM Inc., Armonk, NY, USA). The Shapiro-Wilk test was used to determine the normality of the continuous variables. Comparisons of variables between the groups were made using the Mann-Whitney U-test. Continuous variables were stated as median (IQR) values and categorical variables as number (n) and percentage (%). A p-value of 0.05 was regarded as statistically significant.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

A total of 333 stroke patients who presented at the Emergency Department were examined. Of all the patients, 269 (80.78%) had ischemic stroke and 64 (19.22%) had hemorrhagic stroke. The mean age of the patients was 72.3±12.71 years in the ischemic stroke group and 69.27±14.39 years in the hemorrhagic stroke group. No statistically significant difference was determined between the groups in terms of age.

Of the patients, 163 (48.95%) patients were male and 170 (51.05%) patients were female, with no statistically significant difference between the groups in terms of gender (p=0.079) (Figure 1). The gender distribution in each group showed no statistically significant difference (p=0.308).

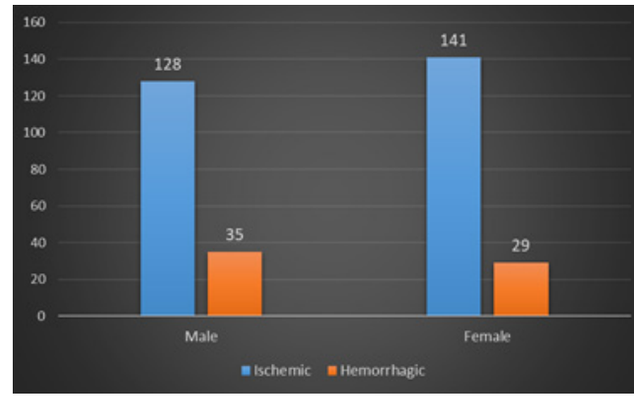

Figure 1. Distribution of sexes according to the groups.

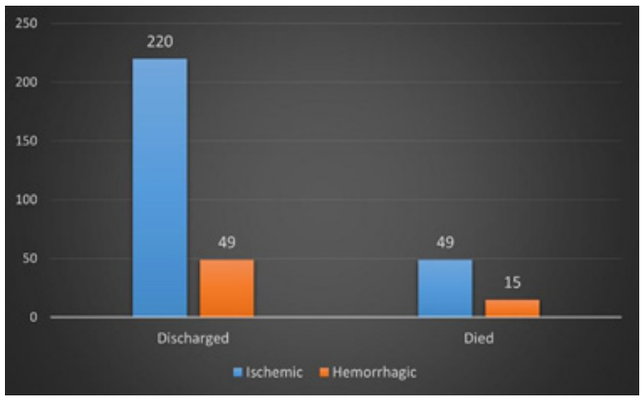

Figure 2. Patient outcomes according to the groups.

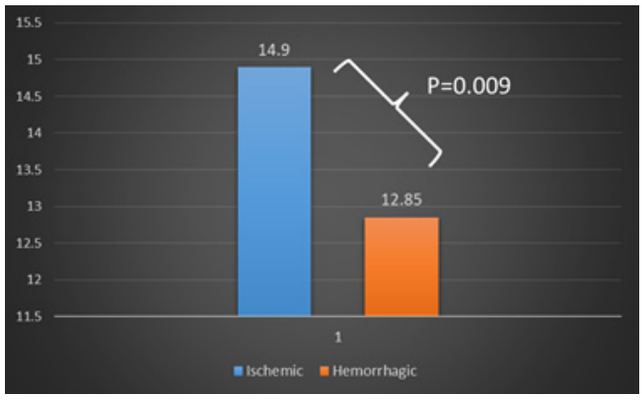

Figure 3. Comparison of PDW between the ischemic and hemorrhagic stroke groups.

Table 1. Comparisons of complete blood count parameters between the groups.

	Ischemic (n=269)	Hemorrhagic (n=64)	p
	Median X [Q1-Q3]	Median X [Q1-Q3]	
WBC; 10^9 /L	8.61 [6.71-11.0]	9.47 [7.72-12.16]	0.051
RBC; 10^{12}/L	4.58 [4.22-4.98]	4.73 [4.42-5.3]	0.031
HGB; g/dL	13.1 [12.1-14.5]	13.9 [12.6-14.98]	0.094
PLT; 10^9 /L	229 [194-284]	226.5 [181.5-289.3]	0.675
MCV; fL	88.10 [84.90-91.35]	87.35 [82.9-89.6]	0.082
RDW; fL	14.6 [13.2-15.9]	14.10 [13.13-15.68]	0.273
LYM; 10^9 /L	1.72 [1.22-2.23]	1.72 [1.14-2.3]	0.774
MONO; 10^9 /L	0.59 [0.45-0.79]	0.58 [0.46-0.75]	0.977
NEU; 10^9 /L	5.60 [4.12-8.1]	6.655 [4.75-9.29]	0.041
BASO; 10^9 /L	0.05 [0.03-0.08]	0.04 [0.02-0.058]	0.001
EOS; 10^9 /L	0.10 [0.04-0.2]	0.09 [0.03-0.16]	0.360
PDW; fL	14.9 [11.9-17.8]	12.85 [11.33-17.03]	0.009
MPV; fL	10.10 [8.43-10.90]	10.30 [9.33-11.0]	0.143
PCT; %	0.22 [0.17-0.28]	0.235 [0.18-0.29]	0.434
CRP; mg/L	5.80 [1.15-14.75]	3.25 [0.5-12.9]	0.166
Albumin; g/L	39.6 [36-42]	41.65 [38.08-44.0]	0.010

Data are shown as median (1st-3rd quartile). WBC: white blood cell count; RBC: red blood cells; HGB: hemoglobin; PLT: platelet count; MCV: mean corpuscular volume; RDW: red cell distribution width; LYM: lymphocyte count; MONO: monocyte count; NEU: neutrophil count; BASO: basophil count; EOS: eosinophil count; MPV: mean platelet volume; PDW: platelet distribution width; CRP: C-reactive protein

The median NIHSS score was 8 (4-15) in the ischemic group and 8 (4-18) in the hemorrhagic group, with no statistically significant difference determined between the groups (p=0.100). The median mRs was measured as 3 (2-5) in the ischemic group, and 4 (2-5) in the hemorrhagic stroke group. The difference between the two groups was not statistically significant (p=0.672). The median GCS score was 13 (9-5) in the patients with ischemic stroke, and 11 (5.25-14.75) in the hemorrhagic stroke group. The median GCS score was statistically significantly higher in the patients with ischemic stroke (p=0.009).

Mortality developed in 66 (19.82%) patients and 268 (80.48%) were discharged. The mortality rate was determined to be 18.22% in the ischemic stroke group and 23.44% in the hemorrhagic stroke group. There was no statistically significant difference between the groups in terms of patient outcomes (p=0.219). The distribution of patient outcomes is shown in Figure 2.

When complete blood count parameters were examined, the median neutrophil count was found to be 5.6 (4.12-8.1) in the ischemic stroke group and 6.66 (4.75-9.29) in the hemorrhagic stroke group. The median neutrophil count was statistically significantly higher in the hemorrhagic stroke group (p=0.041). The median basophil count was found to be 0.05 (0.03-0.08) in the ischemic stroke group, and 0.04 (0.02-0.06) in the hemorrhagic stroke group. There was a statistically significant difference between the ischemic and hemorrhagic stroke groups in respect of basophil count (p=0.001). The median albumin level was found to be 39.6 (36-42) in the ischemic stroke group and 41.65 (38.08-44) in the hemorrhagic stroke group. The difference between the groups in respect of the median albumin value was statistically significant (p=0.010). The median PDW value was found to be 14.9 (11.9-17.8) in the ischemic stroke group, and 12.85 (11.33-17.03) in the hemorrhagic stroke group. The median PDW value was statistically significantly higher in the ischemic stroke group (p=0.009) (Figure 3).

No statistically significant difference was found between the ischemic and hemorrhagic stroke groups in the other parameters (p>0.05 for all) (Table 1).

Discussion

The results of this study showed a statistically significant difference between the ischemic and hemorrhagic stroke groups in terms of PDW. The median PDW was statistically significantly higher in the ischemic stroke group (p=0.009).

The mean age of the patients in this study was 72.3±12.71 years in the patients with ischemic stroke, and 69.27±14.39 years in the patients with hemorrhagic stroke. Tzur et al. investigated PDW as a novel biomarker in internal medicine and reported the mean age of patients to be 66.4 ± 18 years [19]. In another study, Gao et al. evaluated the relationship between poor outcomes of acute ischemic stroke and PDW and found the mean age to be 62.1±12.6 years [20]. Salvadory et al. [6] reported a mean age of 72.9 ± 13.9 years in patients with hemorrhagic and ischemic stroke. Within this context, the current study finding was consistent with previous studies. The gender distribution in the current study was 48.95% male and 51.05% female. Salvadori et al. similarly reported that 52% of

the patients were female and 48% of them were male.

Hemorrhagic stroke is associated with a significantly higher mortality, which is specifically associated with the hemorrhagic nature of the lesion [7]. In the current study, the mortality rate was higher in the hemorrhagic group, although the difference was not statistically significant (p>0.05). Similarly, in a study by Andersen et al. comparing ischemic and hemorrhagic strokes, hemorrhagic stroke was associated with a higher risk of mortality compared to ischemic stroke [7].

Included in routine blood testing, PDW is one of the platelet characteristics that shows platelet activity. An increase in PDW indicates an increase in the number of platelets of various sizes in circulation. Platelets in circulation with a low PDW level have diameters that are closer together, indicating that they are inflammatory and metabolically less active [12]. PDW and MPV are simple platelet indicators that increase during platelet activation. However, PDW is a more specific marker of platelet activation because it does not increase during simple platelet swelling [12]. In addition to other platelet parameters, PDW has been extensively studied in the literature in various diseases. Higher PDW values have been shown in patients with cancer, diabetes mellitus, cardiovascular and cerebrovascular diseases [13,14,21]. Higher PDW values have also been associated with increased morbidity and mortality in patients with coronary artery disease, pulmonary embolism, and COPD [22].

In a study by Tzur et al., higher PDW values on admission to internal medicine wards were associated with an increased risk of 90-day mortality and a more severe clinical prognosis [19]. In another study, Gao et al. reported that a lower level of PDW may be associated with a poor outcome at 3 months following intravenous thrombolysis in patients with acute ischemic stroke [20]. In a study by Al-Tameemi et al., no significant difference was found between 25 patients undergoing the first acute ischemic stroke, 25 patients undergoing more than one ischemic stroke and control groups in terms of PDW [23]. In a study by Li et al., elevated PDW was reported to be an independent indicator of poor functional outcomes in patients with acute ischemic stroke [5]. In contrast, it was reported in a meta-analysis and systematic review by Zheng et al. that PDW has insufficient value in estimating clinical results of acute ischemic stroke [24]. In another study by Sonmezler et al., PDW was reported to be associated with mortality in older patients who had acute ischemic stroke [25].

In the current study, statistically significantly higher PDW values were observed in the patients who had an ischemic stroke compared to those with hemorrhagic stroke. In addition, statistically significant differences were observed between the patients with ischemic stroke and those with hemorrhagic stroke in respect of neutrophil count, basophil count and albumin levels. These results suggest that the PDW index may be used as a novel marker for the differentiation of ischemic and hemorrhagic stroke. However, there is a need for furthermore comprehensive studies to support our findings.

Conclusion

PDW value was seen to be statistically significantly higher in patients who underwent ischemic stroke compared to those who underwent hemorrhagic stroke. PDW may be of value in distinguishing these two forms of stroke. However, further comprehensive, multi-center studies are needed to better understand the role of PDW in ischemic and hemorrhagic stroke.

Study Limitations

Major limitations of this study were that it was conducted in a single center, was retrospective in design, and there was no healthy control group without stroke. However, given the scarcity of similar studies in the literature, these findings can be considered to be of value in guiding further comprehensive studies. However, a strong aspect of the study was that it is the first to have investigated the clinical value of PDW in distinguishing ischemic stroke and hemorrhagic stroke.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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